Advancing practical usage of microtechnology: a study of the functional consequences of dielectrophoresis on neural stem cells.

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Public Summary:
Technologies from the field of engineering that enable rigorous analysis of stem cells hold enormous promise for further unlocking the potential of stem cell based therapies. Determining whether these technologies themselves alter stem cell function is critical to ensure they can be used in a beneficial manner without adversely affecting the cells. For example, engineered systems have been used to investigate neural stem/progenitor cells (NSPCs), which are of interest due to their potential to treat central nervous system disease and injury. Analysis of these cells using dielectrophoresis (DEP) technology determined that unlabeled NSPCs with distinct abilities to form the final differentiated cells of the brain and spinal cord have distinguishing characteristics. These findings suggest NSPCs could be sorted by DEP without the use of cell type specific labels, which would help to enrich populations of cells for therapeutic purposes. To gauge the potential impact of DEP sorting on NSPCs, we investigated whether DEP exposure of varying times affected the survival, ability to divide (proliferation), or ability to differentiate of NSPCs in suspension. We found short-term DEP exposure (1 min or less) had no effect on NSPC survival, proliferation, or differentiation. Moreover, NSPC proliferation (measured by two different methods) and differentiation were not altered by any length of DEP exposure (up to 30 min). However, lengthy exposure (>5 min) to particular DEP frequencies (50–100 kHz) led to decreased survival of NSPCs (maximum ~30% cell loss after 30 min). Based on experimental observations and mathematical simulations of cells in suspension, we find these frequencies generate an induced transmembrane potential that results in cell swelling and rupture. This is in contrast to the case for attached cells since different, lower DEP frequencies generate the highest induced transmembrane potential and damage for cells. We clarify contrasting effects of DEP on attached and suspended cells, which are related to the cell position within the DEP electric field and the strength of the electric field. Modeling predicts optimal designs to induce cell movement by DEP while limiting the induced transmembrane potential. We find DEP electric fields are not harmful to stem cells in suspension at short exposure times, thus providing a basis for developing DEP-based applications for stem cells to improve their use as therapeutics.

Scientific Abstract:
The integration of microscale engineering, microfluidics, and AC electrokinetics such as dielectrophoresis has generated novel microsystems that enable quantitative analysis of cellular phenotype, function, and physiology. These systems are increasingly being used to assess diverse cell types, such as stem cells, so it becomes critical to thoroughly evaluate whether the systems themselves impact cell function. For example, engineered microsystems have been utilized to investigate neural stem/progenitor cells (NSPCs), which are of interest due to their potential to treat CNS disease and injury. Analysis by dielectrophoresis (DEP) microsystems determined that unlabeled NSPCs with distinct fate potential have previously unrecognized distinguishing electrophysiological characteristics, suggesting that NSPCs could be isolated by DEP microsystems without the use of cell type specific labels. To gauge the potential impact of DEP sorting on NSPCs, we investigated whether electric field exposure of varying times affected survival, proliferation, or fate potential of NSPCs in suspension. We found short-term DEP exposure (1 min or less) had no effect on NSPC survival, proliferation, or fate potential revealed by differentiation. Moreover, NSPC proliferation (measured by DNA synthesis and cell cycle kinetics) and fate potential were not altered by any length of DEP exposure (up to 30 min). However, lengthy exposure (>5 min) to frequencies near the crossover frequency (50-100 kHz) led to decreased survival of NSPCs (maximum approximately 30% cell loss after 30 min). Based on experimental observations and mathematical simulations of cells in suspension, we find that frequencies near the crossover frequency generate an induced transmembrane potential that results in cell swelling and rupture. This is in contrast to the case for adherent cells since negative DEP frequencies lower than the crossover frequency generate the highest induced transmembrane potential and damage for these cells. We clarify contrasting effects of DEP on adherent and suspended cells, which

are related to the cell position within the electric field and the strength of the electric field at specific distances from the electrodes. Modeling of electrode configurations predicts optimal designs to induce cell movement by DEP while limiting the induced transmembrane potential. We find DEP electric fields are not harmful to stem cells in suspension at short exposure times, thus providing a basis for developing DEP-based applications for stem cells.

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